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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/632,581

07/31/2003

Anne-Marie Rodriguez

0857/70669

5002

23432 7590 01/26/2009

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EXAMINER

HAMA, JOANNE

ART UNIT

PAPER NUMBER

1632

MAIL DATE

DELIVERY MODE

01/26/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/632,581	Applicant(s) RODRIGUEZ ET AL.	
	Examiner JOANNE HAMA	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 9-12, 25-28, 48 and 51-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 9-12, 25-28, 48 and 51-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant filed a response to the Non-Final Action of June 25, 2008 on September 29, 2008. Claims 6, 8, 13-24, 29-47, 49, 50 are cancelled. Claims 1, 9, 12, 25, 48, 53 are amended.

Claims 1-5, 7, 9-12, 25-28, 48, 51-54, drawn to an isolated adult multipotent human stem cell, are under consideration.

Withdrawn Rejection

35 USC § 112, 2nd parag.

Applicant's arguments, see pages 7-8 of Applicant's response, filed September 29, 2008, with respect to the rejection of claims 1-7, 9-12, 26-28, 48, 51, 52 have been fully considered and are persuasive. Applicant indicates that the claims have been amended to recite "a degree of senescence of less than 0.05% after 60 population doublings." "0.05%" refers to the percentage of cells which are senescent after the claimed cell has undergone 60 population doublings. The rejection of claims 1-5, 7, 9-12, 26-28, 48, 51, 52 has been withdrawn. It is noted that the rejection of claim 6 is withdrawn as the claim has been cancelled.

35 USC § 103

Applicant's arguments with respect to claims 1-5, 7, 9-12, 26-28, 48, 51, 52 being obvious over Katz et al., PCT Publication No. WO 00/53795, publication date, September 14, 2000, previously cited, in view of Akanbi et al., 1994, J. Anim. Sci., 72: 2828-2835, West, US Patent 5,589,483, patented December 31, 1996, have been

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considered, but are moot in view of the new ground(s) of rejection. It is noted that Applicant has amended the claims such that measuring beta-galactosidase in a cell is not required and that the claims are now rejected as obvious over Katz et al., PCT Publication No. WO 00/53795, publication date, September 14, 2000, previously cited, in view of Akanbi et al., 1994, J. Anim. Sci., 72: 2828-2835, Hedrick et al., US Patent Application US 2003/0082152, published May 1, 2003, Haynesworth et al., US Patent 5,733,542, patented March 31, 1998, see below.

Maintained Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9-12, 25-28, 48, 53, 54 remain rejected and claims 1-5, 7, 51, 52 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Katz et al., PCT Publication No. WO 00/53795, publication date, September 14, 2000, previously cited, in view of Akanbi et al., 1994, J. Anim. Sci., 72: 2828-2835, Hedrick et al., US Patent Application US 2003/0082152, published May 1, 2003, Haynesworth et al., US Patent 5,733,542, patented March 31, 1998, for reasons of record, June 25, 2008.

Applicant's arguments filed September 29, 2008 have been fully considered but they are not persuasive.

Applicant indicates that Akanbi et al. teach new born pigs have more preadipocytes capable of attaching and differentiating into mature adipocytes than 7 month old pigs. Akanbi et al. thus teach that adipocyte precursor cells from very young animals may replicate faster than those of older animals and that adipose tissue from young animals may contain more clones capable of full differentiation into adipocytes. This teaches away from the invention. Indeed, Akanbi et al. do not provide any teaching at all relative to stem cells let alone human stem cells. Preadipocytes are a completely different type of cell than stem cells, in particular because they are at a more advanced stage of differentiation and can only differentiate into adipocytes. Applicant indicates that stem cells proliferate more slowly than other cell types (see page 10, lines 2-4 of the specification) and the skilled artisan would not thus use a cell composition which proliferates rapidly because it is very rich in fastly dividing cells, which are not stem cells. Applicant indicates that the teaching of Akanbi et al. is not relevant because it relates to cells which are very different from stem cells in general and even more so from human cells (Applicant's response, page 10). In response, this is not persuasive. The rejection at hand is Katz et al. in view of Akanbi et al. Katz et al. provide guidance on obtaining stem cells from adipose tissues of human. However, Katz et al. do not specifically indicate that the source of cells is from a human that is younger than 10 years. Akanbi et al. provide guidance that the prior art teaches that precursor cells obtained from younger animals replicate faster than cells from older animals and contain more cells that are capable of full differentiation into adipocytes. Given this teaching, an artisan would have modified the teaching of Katz et al. by obtaining cells

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from patients that are younger than adults because cells obtained from younger animals proliferate better and are better at differentiation. With regard to Applicant indicating that the specification teaches that stem cells proliferate more slowly than other cell types (specification, page 10, lines 2-4), this argument is not persuasive because the rejection at hand is that the stem cells obtained by the method of Katz et al., in view of Akanbi et al. proliferate better because they are obtained from humans that are younger than adults.

Applicant indicates that the separation of "CA" cells which are adherent after less than 12 hours from "CS" cells which are adherent after more than 12 hours is an essential feature of the process of preparation of the claimed cells. These two cell types have been shown to have some properties in common, but they also have characteristics that are different from each other. Contrary to what is stated by the Examiner, this process feature is not disclosed by Hedrick et al. Hedrick et al. teach that cells are incubated overnight and that non-adherent red blood cells are eliminated. The term "overnight" is not equivalent to 12 hours. This term should be interpreted as corresponding to at least the time-frame starting when the skilled man, performing work during normal working hours would leave his laboratory, i.e., not later than 6PM and ending when he would arrive in the morning, i.e. not earlier than 8 AM. As such, the term "overnight" should be interpreted as a time-frame of at least 14 hours. In response, this is not persuasive. While "overnight" can be interpreted as 14 hours, "overnight" as 12 hours is as likely an interpretation in the art. For example, Wagner et al., 2004, *Arterioscler. Thomb. Vasc. Biol.*, 24: 715-720 and Kataoka et al., 2003, *Blood*,

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102: 3224-3231 describe overnight as 12 hours (Wagner et al., page 716, 2nd col., 1st parag. under Transmigration Assay; Kataoka et al., Figure 4 legend). As such, an artisan would have reasonably interpreted that "overnight" can mean 12 hours and as such, an artisan would have arrived at CA cells that have adhered to the cell culture dish in less than 12 hours. With regard to Applicant indicating that Hedrick et al. do not teach cells that are adherent after 12 hours, none of the claims are drawn to cells that adhere to a culture dish more than 12 hours after plating.

Applicant indicates that Hedrick et al. state that the non-adherent red blood cells are removed, not that one type of adherent cell is separated from another, as it the case in the process for preparing the claimed cells. The skilled man would thus understand the teaching that this step is performed solely to remove red blood cells (Applicant's response, pages 11-12). In response, this is not persuasive. While Hedrick et al. teach a step of rinsing the cells to remove red blood cells, the step of rinsing is not a specific step that specifically removes red blood cells and leaves behind debris, dead cells, and cells floating in solution.

Applicant indicates that the process described in the specification of the present application is for obtaining the claimed stem cells, wherein the steps comprises a separation step between two cell populations based on the length of time in which they become adherent. This allows separation of CA cells from CS cells. The process also comprises a step of enriching the CA population until a quiescent cell population is obtained. Applicant indicates the step of separating the CA cell population from the CS cell population and the step of enriching the CA population until a quiescent population

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is obtained allows one to eliminate the cells which are not true stem cells. Applicant indicates that Katz et al. did not separate a CA population of cells from a CS population of cells, did not show that the cells they isolated to could enter quiescence, and they differentiated these cells at an early stage. Stem cells are a very rare cell type and the cells isolated by Katz et al. would thus essentially be precursor cells, such as the CS cells disclosed in the invention and not the true stem cells such as that of the CA cells (Applicant's response, pages 12-14). In response, this is not persuasive. As indicated in the Office Action, June 25, 2008, the Examiner acknowledges that Katz et al. do not specifically teach that cells isolated from adipose tissue were allowed to adhere to plates for 12 hours before removing the non-adherent cells. Guidance for allowing cells 12 hours to attach to a surface was taught by Hedrick et al.

Applicant indicates that Katz et al. teach human lipo-derived stem cells which can differentiate into cell types which belong to the limb bud mesoderm (adipocytes, osteocytes, myocytes, and chondrocytes). The cells of the instant invention can not only differentiate into limb bud mesoderm type cells, but also differentiate into visceral mesoderm cell types as well (specification, pages 15-16). As such, the cells of the present invention have a broader differentiation potential than those of Katz et al. (Applicant's response, page 14). In response, this is not persuasive. While Katz et al. do not specifically cells differentiating into visceral mesoderm, lacking this teaching does not indicate that the cells do not have this ability. Rather, Katz et al.'s result indicates that their cells have not been tested for differentiation into this cell type.

Applicant indicates that as already indicated in Applicant's response to the previous Office Action, see section 4.a of the remarks section in the amendment filed in response to the action of February 27, 2007, the cells of Katz et al. do NOT have an endogenous telomerase activity of at least 20-50% of the telomerase activity of the HEK293T cell and which is maintained over at least 130 population doublings (Applicant's emphasis, Applicant's response, page 15). With regard to Applicant's response, April 2, 2008, Applicant indicates that Katz et al. (WO 00/53795) provides no information concerning the level of telomerase activity or whether it is maintained through successive cell passages. Katz et al (WO 00/53795) claims priority to US provisional Application, 60/162,462, provides more detail with regard to the telomerase activity. Applicant indicates that Katz et al.'s priority application teaches that telomerase is measured in a heterogenous primary population of cells (page 40) and there is no disclosure of telomerase activity after 130 population doublings in an isolated multipotent cell as required by the claim. In addition to this, the priority application states that the telomerase activity in the cell population was qualitatively equivalent to a known positive keratinocyte cell line (NHOK) and bone marrow-derived mesenchymal stem cell (page 35) (Applicant's response, April 2, 2008, pages 10-11). Applicant indicates that NHOK cells are normal cells which have a limited life span, exhibit telomerase activity during the proliferative phase, but the telomerase activity is lost near and at senescence. With regard to the second type of cells referred to by Katz et al (WO 00/53795) as being qualitatively equivalent in terms of telomerase activity, i.e., the bone marrow-derived mesenchymal stem cells, the Katz priority document refers to

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Pittenger et al., 1999 and Prockop et al., 1997. The Prockop et al. reference has no reference to telomerase; however, the Pittenger et al. reference does. With regard to Pittenger et al., Zimmerman et al., 2003 refers to the same cells that were used by Pittenger and in their hands, Pittenger et al.'s cells have no telomerase activity. Given these teachings, the cells taught by Katz et al. (WO 00/53795) seem to have, at best, a telomerase activity which is lost after 20 population doublings, or alternatively, no reproducible telomerase activity at all. In response, this is not persuasive. The rejection at hand is Katz et al., in view of Akanbi et al., Hedrick et al., and Haynesworth et al. While Applicant indicates that Katz et al.'s cells are different from that of the claimed invention, the rejection was not solely over Katz et al., but the combination of Katz et al., Akanbi et al., Hedrick et al., and Haynesworth et al. The teaching of Katz et al. and Akanbi et al. leads an artisan to obtain stem cells from adipose tissue of children. With regard to obtaining cells that adhere to the plate over a certain period of time, the art teaches that it is routine to obtain stem cells that adhere to the plate overnight and to remove the cells that do not adhere to the dish (Hedrick et al.). Given the combination of these teachings, an artisan would have arrived at the claimed invention. In addition to this, given that the cells are obtained from children, these cells are not the same as those described by Katz et al. and the analysis of Katz et al.'s telomerase results are not indicative of what occurs in stem cells obtained from adipose tissue of children. While the art does not indicate what characteristics stem cells from adipose tissue of children have, as far as can be told, the combination of references

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leads an artisan to arrive at the claimed cells having the particular characteristics recited in the claims.

Applicant indicates that claims 49 and 50 are cancelled (Applicant's response, page 15). In response, the rejection as it applies to claims 49 and 50 are withdrawn as the claims are cancelled.

Applicant indicates that West (US Patent 5,589,483) does not provide a means to obtain non-senescent cells. West discloses a means to measure senescence, but West does not teach cells which have a degree of senescence of less than 0.05% at 60 population doublings (Applicant's response, page 17-18). In response, as far as can be told, the cells obtained from the teachings of Katz et al., Akanbi et al., Hedrick et al. have a degree of senescence is less than 0.05% at 60 population doublings, for reasons of inherency. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In *re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). It is noted that West had been provided to illustrate that a tool for measuring senescence via a transgene construct

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was known and an artisan would have used this tool to aid in determining the degree of senescence of a cell. It is noted that the claims have been amended and no longer require beta-galactosidase expression from a transgene construct that can be used to measure senescence. As such, West is no longer cited in the 103 rejection, see above.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

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272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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/Joanne Hama/
Primary Examiner
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